Amendments to the specification are indicated in the attached "Marked Up Version of Amendments" (page i).

In the Claims

Please cancel Claims 16, 17, 21, 22, 25, 26 and 29-40. Claims 1, 4-9, 11-15, 18-20, 23, 24, 27, 28 and 41-45 have been amended and are presented below in amended form, and new Claims 46-56 have been added. In accordance with 37 C.F.R. § 1.121(c)(1)(ii), amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages ii-vii).

1. (Amended Five Times) A humanized immunoglobulin or antigen-binding fragment thereof having binding specificity for $\alpha 4\beta 7$ integrin, said immunoglobulin or fragment comprising an antigen-binding region of nonhuman origin and at least a portion of an immunoglobulin of human origin, said antigen-binding region comprising at least one of three complementarity determining regions (CDR1, CDR2 and CDR3) of a light chain variable region and at least one of three complementarity determining regions (CDR1, CDR2 and CDR3) of a heavy chain variable region of the amino acid sequence set forth below such that the antibody specifically binds to the $\alpha 4\beta 7$ integrin:

E3

light chain:	CDR1	amino acids 44-59 of SEQ ID NO: 12
	CDR2	amino acids 75-81 of SEQ ID NO: 12
	CDR3	amino acids 114-122 of SEQ ID NO: 12
heavy chain:	CDR1	amino acids 50-54 of SEQ ID NO: 15
	CDR2	amino acids 69-85 of SEQ ID NO: 15
	CDR3	amino acids 118-129 of SEQ ID NO: 15.

4. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 2 wherein the antigen-binding region is of rodent origin.

E4

5. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 2 comprising:

an immunoglobulin light chain variable region comprising the amino acid sequence of amino acids 21-132 of SEQ ID NO:12; and

E4

an immunoglobulin heavy chain variable region comprising the amino acid sequence of amino acids 20-140 of SEQ ID NO:15.

6. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 1 wherein the portion of an immunoglobulin of human origin is derived from a human framework region.

7. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 6, wherein said immunoglobulin or fragment can compete with Act-1 monoclonal antibody (ATCC Accession No. PTA-3663) for binding to $\alpha 4\beta 7$ integrin.

8. (Amended Five Times) A humanized immunoglobulin or antigen-binding fragment thereof having binding specificity for $\alpha 4\beta 7$ integrin comprising a heavy chain and a light chain,

E5

the light chain comprising complementarity determining regions derived from an antibody of nonhuman origin which binds $\alpha 4\beta 7$ and a framework region derived from a light chain variable region of human origin, wherein each of said complementarity determining regions (CDR1, CDR2 and CDR3) comprises the amino acid sequence set forth below:

light chain: CDR1 amino acids 44-59 of SEQ ID NO: 12
CDR2 amino acids 75-81 of SEQ ID NO: 12
CDR3 amino acids 114-122 of SEQ ID NO: 12; and

the heavy chain comprising complementarity determining regions derived from an antibody of nonhuman origin which binds $\alpha 4\beta 7$ and a framework region derived from a heavy chain variable region of human origin, wherein each of said complementarity

determining regions (CDR1, CDR2 and CDR3) comprises the amino acid sequence set forth below:

E5

heavy chain: CDR1 amino acids 50-54 of SEQ ID NO: 15
CDR2 amino acids 69-85 of SEQ ID NO: 15
CDR3 amino acids 118-129 of SEQ ID NO: 15.

9. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 8 wherein said immunoglobulin can compete with murine Act-1 monoclonal antibody (ATCC Accession No. PTA-3663) for binding to $\alpha 4\beta 7$.

E6

11. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 8 wherein said light chain variable region of human origin is the light chain variable region of the human GM607'CL antibody (SEQ ID NO: 8).

12. (Twice Amended) The humanized immunoglobulin or antigen-binding fragment of Claim 8 wherein said heavy chain variable region of human origin is the heavy chain variable region of the human 21/28'CL antibody (SEQ ID NO: 10).

13. (Amended Five Times) A humanized immunoglobulin light chain or antigen-binding portion thereof comprising complementarity determining regions (CDR1, CDR2 and CDR3) of the light chain of murine Act-1 antibody (ATCC Accession No. PTA-3663), and a framework region derived from a light chain variable region of human origin, said complementarity determining regions comprising the amino acid sequences set forth below such that an antibody or antigen-binding fragment thereof comprising said light chain or antigen-binding portion thereof specifically binds to the $\alpha 4\beta 7$ integrin:

E7

light chain: CDR1 amino acids 44-59 of SEQ ID NO: 12
CDR2 amino acids 75-81 of SEQ ID NO: 12
CDR3 amino acids 114-122 of SEQ ID NO: 12.

14. (Twice Amended) The humanized immunoglobulin light chain or antigen-binding portion thereof of Claim 13 wherein the human framework region is derived from the light chain variable region of the human GM607'CL antibody (SEQ ID NO: 8).

E8

15. (Twice Amended) The humanized immunoglobulin light chain or antigen-binding portion thereof of Claim 14 comprising the variable region of SEQ ID NO:21.

18. (Amended Five Times) A humanized immunoglobulin heavy chain or antigen-binding portion thereof comprising complementarity determining regions (CDR1, CDR2 and CDR3) of the heavy chain of the murine Act-1 antibody (ATCC Accession No. PTA-3663), and a framework region derived from a heavy chain variable region of human origin, said complementarity determining regions comprising the amino acid sequences set forth below such that an antibody or antigen-binding fragment thereof comprising said heavy chain or antigen-binding portion thereof specifically binds to the $\alpha 4\beta 7$ integrin:

E9

heavy chain: CDR1 amino acids 50-54 of SEQ ID NO: 15
CDR2 amino acids 69-85 of SEQ ID NO: 15
CDR3 amino acids 118-129 of SEQ ID NO: 15.

19. (Twice Amended) The humanized immunoglobulin heavy chain or antigen-binding portion thereof of Claim 18 wherein the human framework region is derived from the heavy chain variable region of the human 21/28'CL antibody (SEQ ID NO: 10).

E10

20. (Twice Amended) The humanized immunoglobulin heavy chain or antigen-binding portion thereof of Claim 19 comprising the variable region of SEQ ID NO:19.

23. (Amended Three Times) A humanized immunoglobulin light chain, the amino acid sequence of said light chain comprising at least an antigen-binding portion of the light chain variable region amino acid sequence shown in Figure 7 (amino acids 21-132 of SEQ ID NO:12).

24. (Twice Amended) The humanized immunoglobulin light chain of Claim 23, wherein said amino acid sequence of said light chain comprises the signal peptide sequence shown in Figure 7 (amino acids 1-20 of SEQ ID NO:12) and at least an antigen-binding portion of the light chain variable region amino acid sequence shown in Figure 7 (amino acids 21-132 of SEQ ID NO:12).

E11

27. (Amended Three Times) A humanized immunoglobulin heavy chain, the amino acid sequence of said heavy chain comprising at least an antigen-binding portion of the heavy chain variable region amino acid sequence shown in Figure 9 (amino acids 20-140 of SEQ ID NO:15).

28. (Twice Amended) The humanized immunoglobulin heavy chain of Claim 27, wherein said amino acid sequence of said heavy chain comprises the signal peptide sequence shown in Figure 9 (amino acids 1-19 of SEQ ID NO:15) and at least an antigen-binding portion of the heavy chain variable region amino acid sequence shown in Figure 9 (amino acids 20-140 of SEQ ID NO:15).

41. (Amended) A method of inhibiting the interaction of a first cell bearing $\alpha 4\beta 7$ with a second cell bearing a ligand thereof, comprising contacting said first cell with an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 1.

E12

42. (Amended) A method of inhibiting leukocyte infiltration of mucosal tissue, comprising administering to a patient an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 1.

43. (Amended) A method of therapy of a disease associated with leukocyte infiltration of tissues expressing the molecule MAdCAM-1, comprising administering to a patient an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 1.

E12

44. (Amended) The method of Claim 43, wherein the disease is a disease associated with leukocyte infiltration of tissues as a result of binding of leukocytes to gut-associated endothelium expressing the molecule MAdCAM-1.

45. (Amended) A method for treating inflammatory bowel disease in a patient, comprising administering to the patient an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 1.

46. (New) A method of inhibiting the interaction of a first cell bearing $\alpha 4\beta 7$ with a second cell bearing a ligand thereof, comprising contacting said first cell with an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 8.

E13

47. (New) A method of inhibiting leukocyte infiltration of mucosal tissue, comprising administering to a patient an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 8.

48. (New) A method of therapy of a disease associated with leukocyte infiltration of tissues expressing the molecule MAdCAM-1, comprising administering to a patient an effective amount of a humanized immunoglobulin or antigen-binding fragment of Claim 8.

49. (New) The method of Claim 48, wherein the disease is a disease associated with leukocyte infiltration of tissues as a result of binding of leukocytes to gut-associated endothelium expressing the molecule MAdCAM-1.

50. (New) A method for treating inflammatory bowel disease in a patient, comprising administering to the patient an effective amount of a humanized immunoglobulin or antigen-binding fragment thereof having binding specificity for $\alpha 4\beta 7$ integrin comprising a heavy chain and a light chain, wherein:

said light chain comprises complementarity determining regions (CDR1, CDR2 and CDR3) derived from an antibody of nonhuman origin which binds $\alpha 4\beta 7$ and a framework region derived from a light chain variable region of human origin, wherein said complementarity determining regions (CDR1, CDR2 and CDR3) comprise the amino acid sequences set forth below:

E13

light chain: CDR1 amino acids 44-59 of SEQ ID NO: 12
CDR2 amino acids 75-81 of SEQ ID NO: 12
CDR3 amino acids 114-122 of SEQ ID NO: 12; and

said heavy chain comprises complementarity determining regions (CDR1, CDR2 and CDR3) derived from an antibody of nonhuman origin which binds $\alpha 4\beta 7$ and a framework region derived from a heavy chain variable region of human origin, wherein said complementarity determining regions (CDR1, CDR2 and CDR3) comprise the amino acid sequences set forth below:

heavy chain: CDR1 amino acids 50-54 of SEQ ID NO: 15
CDR2 amino acids 69-85 of SEQ ID NO: 15
CDR3 amino acids 118-129 of SEQ ID NO: 15.

51. (New) The method of Claim 50 wherein said inflammatory bowel disease is ulcerative colitis.

52. (New) The method of Claim 50 wherein said inflammatory bowel disease is Crohn's disease.

53. (New) A humanized immunoglobulin or antigen-binding fragment thereof having binding specificity for α4β7 integrin comprising a heavy chain and a light chain, wherein said heavy chain comprises the variable region of SEQ ID NO:19 and said light chain comprises the variable region of SEQ ID NO:21.

E13

54. (New) A method for treating inflammatory bowel disease in a patient, comprising administering to the patient an effective amount of a humanized immunoglobulin or antigen-binding fragment thereof having binding specificity for α4β7 integrin comprising a heavy chain and a light chain, wherein said heavy chain comprises the variable region of SEQ ID NO:19 and said light chain comprises the variable region of SEQ ID NO:21.

55. (New) The method of Claim 54 wherein said inflammatory bowel disease is ulcerative colitis.

56. (New) The method of Claim 54 wherein said inflammatory bowel disease is Crohn's disease.

REMARKS

Amendments to the Specification

The Specification has been amended to refer to biological material (murine Act-1 hybridoma cell line which produces the murine Act-1 monoclonal antibody) described in the application as filed and subsequently deposited under the Budapest Treaty at the American Type Culture Collection (ATCC). As required by 37 C.F.R. § 1.809(d), the Specification has been amended to recite: (a) the accession number of the deposit; (b) the date of deposit; and (c) the name and address of the depository. A copy of the ATCC Deposit Receipt and Viability Statement for murine hybridoma Act-1 is provided herewith.

A Statement under 37 C.F.R. § 1.804(b) and a Statement under 37 C.F.R. § 1.806 and § 1.808 are being filed concurrently, completing the formal requirements for the biological deposit.